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TITLE PAGE

Effect of Sugar-Sweetened Beverages on Oral Health: A Systematic Review and Meta-Analysis

Maria J. Valenzuela,[1] Beverley Waterhouse,[1] Vishal R. Aggarwal,[2] Karen Bloor,[1] Tim Doran[1]

1. Department of Health Sciences, University of York, UK (institution to which the work should be attributed)

2. School of Dentistry, University of Leeds, UK

Correspondence author:

Maria Josefina Valenzuela

Department of Health Sciences
University of York
Heslington
York
UK
YO10 5DD
+447580141085

ABSTRACT

Background: The impact of consumption of sugar-sweetened beverages (SSB) on health outcomes such as obesity have been studied extensively, but oral health has been relatively neglected. This study aims to assess the association between SSB consumption and dental caries and erosion.

Methods: Systematic review of observational studies. Search strategy applied to Medline, Embase, Cochrane Library, SciELO, LILACS, OpenGrey and HMIC. The risk of bias was assessed using the NIH Quality Assessment Tool for Observational Cross-Sectional Studies and evidence certainty using GRADE. Relationships between SSB consumption and caries and erosion were estimated using random-effects model meta- and dose-response analyses.

Results: 38 cross-sectional studies were included, of which twenty-six were rated as high quality. Comparing moderate to low consumption, there was significantly increased risk of both caries (OR=1.57, 95%CI: 1.28-1.92; DMFT WMD=0.82, 95%CI: 0.38-1.26) and erosion (OR=1.43, 95%CI: 1.01-2.03). Comparing high to moderate consumption, there was further increased risk of caries (OR=1.53, 95%CI: 1.17-1.99; DMFT WMD=1.16, 95%CI: -0.59-2.91) and erosion (OR=3.09, 95%CI: 1.37-6.97). A dose-response gradient and high certainty of evidence was observed for caries.

Conclusions: Increasing SSB consumption is associated with increased risk of dental caries and erosion. Studies were cross-sectional, hence temporality could not be established, but the positive dose-response suggests this relationship is likely to be causal. These findings illustrate the potential benefits to oral health of policies that reduce SSB consumption, including sugar taxation.

INTRODUCTION

The association between consumption of sugar-sweetened beverages (SSB) and adverse health outcomes has been extensively reported in the literature.[1-5] Authors generally focus on weight gain and obesity, giving little attention to oral health despite the existence of two preventable and highly prevalent oral health problems that are associated with diet: dental caries and erosion. The World Health Organization has estimated that dental caries affects between 60 and 90% of schoolchildren and the vast majority of adults.[6] The prevalence of dental erosion varies greatly in the literature and across countries, but reports show that up to three-quarters of the population present some degree of tooth erosion worldwide.[7,8] Among many consequences, these conditions may lead to pain, discomfort, disfigurement, acute and chronic infections, and eating and sleeping disruption as well as higher risk of hospitalisation, high treatment costs and lost work/school days.[9,10] For children, caries affects nutrition, growth and weight gain.[10]

SSB have been implicated as important risk factors for adverse oral health as they contain large quantities of sugar and are highly acidic, and therefore contribute to the development of dental caries and tooth erosion.[11-13] Dental caries is caused by endogenous bacteria that produce acid from the metabolism of carbohydrates, e.g., sugar, whereas tooth erosion is caused by intrinsic and extrinsic acids, e.g., gastro-oesophageal reflux and SSB. An acidic environment in the oral cavity, below the critical pH (5.5) at which enamel demineralisation occurs, results in loss of the tooth surface if left unchecked.[3,14] SSB include the full spectrum of soft drinks, fruit drinks, and energy and vitamin water drinks. They are non-alcoholic, carbonated or non-carbonated and may contain naturally derived sweeteners such as sucrose and glucose, or artificial sweeteners such as aspartame. Their consumption has tripled worldwide in the last 50 years, and this trend has been associated with increasing

prevalence of many non-communicable diseases, such as metabolic syndrome, type-2 diabetes and cardiovascular disease.[1,11]

Although some studies have investigated the association between SSB consumption and oral health,[5,15-18] the evidence has not been pooled quantitatively. Knowledge of the strength of effect would be beneficial for policymakers aiming to design public policies to reduce SSB consumption, including sugar taxation, which aims to reduce consumption by increasing SSB prices. The aim of this systematic review is therefore to determine the strength of association between consumption of different levels of SSB and dental caries and erosion in the general population by conducting meta-analyses, dose-response analyses and appraisal of the quality of evidence.

METHODS

The study addressed the following research question: in the general population, is consumption of higher levels of sugar-sweetened beverages compared with lower levels of consumption, associated with dental caries and/or dental erosion, and what is the strength of the association? To answer this, a systematic review and meta-analysis were undertaken following PRISMA guidelines for systematic reviews,[19] and the protocol was registered in the PROSPERO database (registration number CRD42018088720).

Search strategy

Studies were identified through electronic searches, and from reference lists of included papers. A preliminary search in Web of Science was undertaken to avoid duplication of reviews. A systematic search was conducted up to 17th October 2017 in MEDLINE (Ovid), EMBASE (Ovid), Cochrane Library (Wiley), SciELO (Web of Science) and LILACS (VHL). HMIC (Ovid) and Open Grey were also included to search for grey literature to minimise the risk of publication bias. Supplementary table S1 provides an example search strategy.

Terms related to SSB (for example, soft drink$) and oral health (for example, dental caries OR dental erosion) were used. Terms were generated based on words commonly used in the related literature. Synonyms, abbreviations and alternative spellings were outlined, and then the appropriateness of the selected terms was discussed within the research team.

Different techniques were used to obtain an appropriate balance between sensitivity and specificity.[20] The Boolean operators 'OR' and 'AND' were used to combine similar terms within and between each group. Truncation and wildcards were used to expand terms to include different versions of words with a common root. The proximity operator 'adj3' was used to specify that two search terms should be adjacent to each other within three words. MeSH terms were used in combination with free text terms to identify as many relevant records as possible. No restrictions on publication date, country setting, publication type/status and language were applied. Terms were adapted for each database, and the searches were piloted.

Eligibility criteria

Using the PICOS strategy (Population, Intervention/Exposure, Comparison, Outcomes, Type of Study),[21] studies were included if they met the following criteria: participants from general populations; consumption of any type of SSB; high SSB consumers compared to a lower consumption group including non-consumers; dental caries (measured by the decayed, missing and filled teeth or surfaces indices for primary or adult teeth (DMFT/dmft or DMFS/dmfs), or by the early childhood caries (ECC) index), and/or dental erosion (no restriction in measurement as no general consensus on a standard index has been reached by dental academics) measured at two or more SSB consumption levels. Randomised controlled trials (RCTs), quasi-experimental studies, observational studies, and natural experiments were included. Single case-studies, qualitative studies, in-vitro studies, animal studies, reviews,

editorials, opinion letters and conference abstracts or posters were excluded. Articles published in English and Spanish were included.

All references were exported into EndNote version X8.0.1, where duplicated records were identified and removed. Two researchers (M.J.V. & B.W.) independently screened titles and abstracts against the inclusion and exclusion criteria. Full texts of potentially relevant studies were then retrieved and examined for inclusion. Disagreements between reviewers were resolved through discussion and consensus. Level of agreement between reviewers was assessed with Kappa Cohen in STATA version 15.1.[22]

Data extraction

The data extraction form was based on Centre for Reviews and Dissemination guidance.[20] One researcher extracted data from included studies, and a second researcher checked the extraction. Disagreements were resolved through discussion and consensus. When relevant data were missing, or reporting was inconsistent, study authors were contacted for more details. Information extracted from each study included: main author(s) name(s); year and journal of publication; study design; country; population and participants' characteristics (including age, type of dentition and gender); sample size; type of drink, and measure of consumption (level of consumption and portion size); and type of outcome and method of measurement.

Risk of bias assessment

Two reviewers assessed the risk of bias of the included studies independently. Disagreements were resolved through discussion and consensus; however, if consensus was not achieved, a third reviewer was consulted. Risk of bias was assessed using a modified version of the NIH Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies.[23] Rather than providing a numeric score, this tool was designed to critically appraise the internal validity of studies by focusing on the sample characteristics, recruitment process, and the level of in-

depth reported information of the exposure and outcome measures. Each study was assessed as 'Good', 'Fair' or 'Poor'. Studies were not excluded based on their rating.[20]

Data analysis

As every study measured SSB consumption differently, levels of consumption were categorised as Low, Moderate and High (see Supplementary table S2). A common portion size (250ml) was applied to all studies and converted to millilitres per day (ml/day).[24] For studies that reported consumption as "times a week", it was assumed that "times" were equal to servings of 250ml.[25,26] Finally, for studies that presented SSB consumption in categories with intervals, a midpoint of the lower and upper boundaries was recorded. For the lowest categories with open-ended intervals, zero consumption was assigned as the lower boundary, and for upper categories with open-ended intervals, the upper boundary was assumed to be 20% higher than the lower boundary.[27,28]

Data synthesis

Meta-analyses were conducted for each oral health outcome using a random-effects model.[29] For binary and continuous outcomes, odds-ratios (OR) and weighted mean differences (WMD) respectively were computed to estimate the effect of SSB consumption on oral health. Data were pooled in four meta-analyses comparing none/low with moderate consumption, none/low with high consumption, moderate with high consumption and none/low with moderate/high levels of consumption for each outcome measure.

Subgroup analyses were undertaken by type of dentition (primary, mixed or permanent) to examine changes on the effect size from early ages to adulthood. If the studies did not report type of dentition, this information was inferred from the age of the study sample.[30]

Between-studies heterogeneity was explored using chi-squared Cochran's Q test of heterogeneity and I^2 statistic (p<0.05).[31,32]

Dose-Response Analysis

Risk-ratios (RR) were used to estimate the effect size in the dose-response analysis between SSB and dental caries, measured using a two-stage generalised least squares trend estimation.[25,28,33] The regression coefficient was calculated for every study, and pooled in a multivariate random-effects model to estimate the average slope. Levels of SSB consumption were modelled using restricted cubic splines with four knots at 5%, 35%, 65%, and 95% percentiles of the distribution. P<0.05 was considered statistically significant for all analyses. A likelihood ratio test was performed to compare the difference between linear and non-linear models. Only studies reporting three or more categories of SSB consumption were included in this analysis. A dose-response analysis was not undertaken for erosion as not enough studies met the inclusion criteria. Analyses were conducted in Stata version 15.

Additional analyses

Publication bias was examined visually using funnel plot asymmetry and formally using Egger's asymmetry test (p<0.05).[34] Influence analyses were conducted to examine the potential effect of each study on the pooled effect sizes. Two sensitivity analyses were undertaken; first exploring variation in estimates assuming a portion size of 330 ml rather than 250 ml, as this is the volume of a regular-sized SSB can; and second to evaluate the robustness of the pooled dose-response curve against the assumptions and decisions taken *a priori*. In the spline model, sensitivity analyses assessed the effect of alternative knot locations on the shape of the dose-response curve.

Quality of evidence

Using the Grading of Recommendation Assessment Development and Evaluation (GRADE) tool, we assessed the quality and certainty of the body of evidence.[35] The programme GRADEpro GDT 2015 was used to generate a certainty of evidence table (Table 2). Starting from a high-quality level, it was downgraded according to the presence of limitations in the risk of bias, study design, consistency, or precision of the pooled estimate. The quality level was then rated as high, moderate, low or very low according to the limitations.

RESULTS

Study selection

A total of 3511 studies were identified for inclusion in the review. After excluding duplicates, 1940 citations were screened. Of these, 1552 titles were excluded because they did not meet the eligibility criteria. The full text of 388 citations were retrieved and examined against the inclusion and exclusion criteria in detail and 287 studies were excluded at this stage because they did not assess the relationship between SSB consumption and oral health or did not report sufficient data for the analyses. Fifteen studies were posters, conference abstracts or reviews. Forty were not found or were not accessible. For these studies, authors were contacted to gain access, but limited responses were received. Finally, 38 studies met the eligibility criteria (Figure 1). The Kappa Cohen statistic indicated a high interrater reliability (k=0.8).

[Figure 1 – PRISMA Flowchart about here]

Study characteristics

The majority of studies were undertaken in Asia (22 studies) followed by North and South America (six studies), Europe (four studies), Australia (four studies) and Africa (two studies). Most studies used a cross-sectional design except for three that used baseline and final records of cohort studies. Twenty-one studies involved adults with permanent dentition, nine included young children with primary dentition and eight young adolescents with mixed dentition. SSB consumption was assessed through structured questionnaires. Most studies included sweetened carbonated drinks as the exposure; however, one assessed consumption of only sport drinks and two pooled carbonated drinks with juices or sparkling water. A greater number of studies measured dental caries (23 studies) compared to erosion (14 studies). Only one study reported both outcomes. Twenty out of 24 studies used the

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DMFT/dmft index, where participants with a score equal to zero were categorised as caries-free and participants with a score greater or equal to one were categorised as having caries. The other four studies did not report any specific index when measuring the presence of caries. Various indexes were used to measure the presence or absence of erosion across studies. Three studies used the Tooth Wear Index (TWI), three its modified version, two the Basic Erosive Wear Examination (BEWE), two the O'Sullivan index, one the Visual Erosion Dental Examination (VEDE) and four did not report any specific index. See the Supplementary table S3 for more details.

Risk of bias within studies

Overall, the evidence of the relationship between SSB consumption and the oral health outcomes was of a good quality level. Twenty-six studies were rated as 'Good', nine as 'Fair' and three as 'Poor'. In general, 'Poor' studies failed to provide an appropriate description of the sample, eligibility criteria and size, and they did not explore different levels of SSB consumption. See the Supplementary table S4 for a summary of the quality assessment undertaken for each study.

Effect of SSB consumption on dental caries

Meta-analyses

Twenty studies were included in the meta-analyses to estimate the odds of having caries, and eleven studies were included to estimate the difference in mean DMFT/dmft. Most OR and WMD random-effects meta-analyses revealed a statistically significant association between SSB consumption and caries. As Table 1 shows, moderate consumers have significantly higher odds of caries (OR=1.72, 95%CI: 1.41-2.09, p=0.0001), and have on average 1.22 more decayed, missed or filled teeth than never/low-level consumers (95%CI: 0.48-1.96,

p=0.0001). There is a clear effect difference between types of dentition. The OR is higher in primary dentition compared to permanent dentition; however, it improves during the mixed dentition phase. By contrast, the WMD is slightly lower in the primary dentition compared to the permanent dentition but decreases during the mixed dentition phase.

The OR and WMD for caries are similar between never/low to moderate level and moderate level to high level consumers (OR=1.57, 95%CI: 1.28-1.92, p=0.0001 and WMD=0.82, 95%CI: 0.38-1.26, p=0.0001; OR=1.53, 95%CI: 1.17-1.99, p=0.0001 and WMD=1.16, 95%CI: -0.59-2.91, p=0.0001, respectively). However, the odds of having caries and the WMD among high-level consumers are almost twice that of never/low-level consumers (OR=1.95, 95%CI: 1.57-2.41, p=0.017; WMD=1.91, 95%CI: -0.94-4.75, p=0.0001). Overall, the OR in primary dentition is higher than permanent dentition, and in contrast, the WMD is more severe during adulthood compared to early years. See figures S1 to S4 in the Supplementary material for forest and funnel plots, and a summary of the effect of SSB consumption on caries and erosion.

[Table 1 - Meta-analyses effect summary about here]

Dose-response analysis

Ten studies were included in the dose-response analysis. Linear and non-linear dose-response associations between the amount of SSB consumption and the risk of dental caries were explored; the likelihood test revealed that the relationship is non-linear. Figure 2 shows that the risk of caries is steeper as the amount of SSB increases up to 150ml/day, and then levels (see the Supplementary table S5 for the risk estimate and 95% CI for each quantity of SSB).

Effect of SSB consumption on dental erosion

Meta-analyses

Fifteen studies were included in the meta-analyses that estimate the effect of SSB consumption on dental erosion. Overall, the OR random-effects meta-analyses revealed statistically significant effects of SSB consumption on erosion. Table 1 shows that the odds of having erosion for those who drink more than two portions of SSB a week are more than two-thirds higher than the odds of erosion for those who do not consume or drink less than that amount (OR=1.77, 95%CI: 1.28-2.43, p=0.0001). Similar to caries, there is a clear effect difference across types of dentition; however, for erosion, the OR is lower in the primary compared to permanent dentition. The odds of having erosion among high SSB consumers are three times the odds of both moderate and never/low-level consumers (OR=3.09, 95%CI: 1.37-6.97, p=0.0001; OR=2.9, 95%CI: 1.32-6.4, p=0.0001), whereas between never/low and moderate level consumers this estimate is lower, but still significant (OR=1.43, 95% CI: 1.01-2.03).

Risk of bias across studies and additional analyses

Funnel plots showed evidence of considerable asymmetry (See Figures 2A, B and C in the Supplementary material). To account for this heterogeneity, all meta-analyses were undertaken using a random-effects model. Egger's asymmetry test showed no publication bias in the meta-analyses, suggesting no major threat to validity. No study demonstrated a large effect on the influence analyses. The sensitivity analyses showed no substantial variation in the estimates.

Certainty of the evidence

The certainty of the evidence was high for dental caries and most of the erosion subgroup meta-analyses using GRADE criteria (Table 2). Subgroups analysed using DMFT scores showed a moderate certainty of evidence whereas those assessed as a presence/absence of the outcome showed a high certainty. The main drivers for a high certainty of evidence were the strength of effect (particularly for erosion outcomes), the dose-response gradient for the caries outcome and lack of publication bias.

[Table 2 – GRADE summary about here]

DISCUSSION

Summary of main findings

Although other reviews have found an association between SSB and caries and erosion, to our knowledge, our study is the first to quantify this relationship using different levels of consumption. We found not only a positive association but also a dose-response gradient between SSB consumption and caries. Our analyses show that people who consume larger quantities of SSB (daily or several times a week) have greater odds of having dental caries and erosion, and higher caries rates than people who consume smaller amounts (less than twice a week). The evidence was robust in establishing these relationships given the lack of publication bias, quality of studies, the strength of the effect and the dose-response relationship found between SSB and caries and erosion.

Comparison with previous reviews

Our findings are consistent with other reviews.[5,12,15-18] However, previous studies compare the effect of no consumption with absolute consumption of SSB, or provide a narrative analysis.

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While the majority conclude that there is substantial evidence supporting an association between SSB consumption and caries and erosion,[15-18] there is uncertainty regarding the strength, with one review[5] claiming (based on results from four studies) that although this association is positive, it is small (r=0.03). Existing reviews are somewhat unclear about the amount of SSB considered in their analyses. Salas et al. (2015)[18] for example, report that higher consumption levels of SSB are associated with erosion, but the authors do not define 'high' levels of consumption. Similarly, while Li et al. (2012)[17] report that the OR for SSB consumption and erosion is 2.41 (similar to our findings) they do not clarify the amounts of SSB being compared. The findings of our review corroborate these positive associations between SSB and caries and erosion, but go further by quantifying the relationships more precisely, based on amounts of SSB consumed.

Strengths and limitations

The main strength of our review is that it quantifies the association between different levels of SSB consumption and caries and erosion, providing a dose-response relationship. Additionally, our review includes studies from a variety of countries (twenty-two) and provides a detailed assessment of the characteristics of the included studies showing the quality and certainty levels of the evidence. The certainty of evidence was assessed for each outcome using the GRADE approach, which was rated strong for dental caries and most of the erosion subgroup meta-analyses and moderate for the subgroup analyses using DMFT scores. These certainty levels were shaped by the strong effects found in the analyses, the low risk of bias in the majority of the studies and the lack of publication bias. These levels assure that the findings of this review are robust and can inform future public health policies regarding SSB consumption and oral health.

Although the studies included in this review were cross-sectional, and therefore cannot inform temporal relationships as longitudinal studies would,[20] the established

biological plausibility of the relationship between sugar consumption and caries,[13] along with the strength of association and dose-response relationship observed in our review, suggest that the relationship between SSB consumption and dental carries is likely to be causal.[36]

From the included studies, a greater number of articles measured dental caries as the primary oral health outcome compared to erosion, which may be due to the lack of a standardised tool for data collection.[37] Unlike with caries, researchers have still not reached consensus on a common method to quantify and measure erosion, and studies used different methods, making comparisons between them problematic. Consequently, this may have introduced heterogeneity in the erosion meta-analyses.

We also found a lack of consensus on a standardised tool to collect information on SSB consumption as evidenced by the variability in questionnaires used to collect the data. For this reason, we standardised the various SSB measurements by using methods employed in other studies.[24,26,38-39] This approach has been found adequate and useful; however, given that researchers reported limited information on the accuracy, validity and reliability of their questionnaires, the method of measurement of each study and the standardisation approach may have over or underestimated the results. Sensitivity analyses were undertaken to explore the effect of the standardisation approach on the results, including the use of different portion sizes and alternative combinations in the dose-response analysis; however, the relationships observed between SSB and caries and erosion remained unchanged.

There are, however, some further limitations to consider. First, the data extracted from the studies were unadjusted for potential confounders, as only a few studies provided additional information about contextual factors, such as socio-economic status and fluoridated water. Second, some studies did not differentiate between the type of beverage, e.g., sparkling juices or sports drinks, instead reporting combined data for all carbonated beverages, which could have introduced some measurement bias as different beverages have different levels of pH and added sugar. Also, the actual doses of sugar and acid in the portions of SSB were not

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reported, which could have led to some degree of misclassification as some beverages categorised as sugar-sweetened beverages may have contained natural sweeteners. Finally, we restricted our search to papers in English and Spanish, the languages spoken natively by the research team. We may therefore have missed key papers published in other languages.

Implications for policy and future research

The findings of this review support public health concerns about the implications of SSB consumption on health and are in line with other studies that have aimed at informing international guidelines for sugar consumption, such as the study undertaken by Moynihan and Kelly.[13] As well as potentially reducing overweight and obesity, successful efforts to discourage the consumption of SSB are likely to lead to the prevention of two of the leading causes of morbidity worldwide, dental caries and erosion. Interventions to reduce the consumption of SSB are a valuable addition to oral health prevention efforts and may result in large population benefits.

Although a number of studies provide data on the association of SSB with dental caries and erosion, further research using well-designed controlled studies exploring the effect of different types of SSB, in different age groups, especially in older age groups as caries and erosion are cumulative diseases, and taking into account important confounders such as socio-economic status, are needed. The included studies show that there is a large variety of methods of SSB measurement. There is need for a standardised method to quantify and measure SSB consumption, as has been implemented in research on alcohol consumption,[40] to facilitate future research in this area and to enable public health officials to use this evidence for the development of guidelines and intake recommendations across populations.

Conclusions

This review demonstrates that SSB consumption is a significant risk factor for dental caries and erosion and that the strength of the relationship between these outcomes and the exposure depends on the level of consumption with a clear dose-response relationship between SSB consumption and dental caries. The current body of evidence surrounding the effect of SSB consumption on oral health is consistent with the literature, of good quality and certainty and provides a timely opportunity to inform future public health policies to reduce SSB consumption, including sugar taxation.

FUNDING

CONFLICTS OF INTEREST

None declared.

KEY POINTS

- The effect of sugar-sweetened beverage (SSB) consumption on health is well known, yet, the effect of different levels of consumption on oral health is still unclear.

- This systematic review shows that those consuming SSB daily or several times-a-week have greater odds of having dental caries and erosion than people who consume SSB less than twice-a-week.

- While these findings are consistent with other reviews, ours go further, increasing the robustness of the evidence by quantifying the relationship more precisely, as it considers three levels of SSB and uses dose-response meta-analysis methods.

- As well as potentially reducing weight problems, successful efforts to discourage the consumption of SSB are likely to lead to the prevention of two of the leading causes of morbidity worldwide, dental caries and erosion and provide a timely opportunity to inform future public health policies to reduce SSB consumption, including sugar taxation.

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Table 1. Summary of the effect of SSB on caries and erosion using random-effects model

SSB levels comparison	Outcome	Overall estimation/ Type of dentition	No. of studies	N	Effect size (95% CI)	I^2 (%)
Never/Low vs Moderate	Caries	Overall OR	16	13919	1.57 (1.28-1.92)	73.7
		Primary dentition	4	5500	2.57 (1.70-3.89)	51.6
		Mixed dentition	2	2618	1.15 (0.59-2.27)	93.7
		Permanent dentition	10	5801	1.44 (1.20-1.73)	42.2
		Overall WMD	9	6131	0.82 (0.38-1.26)	83
		Primary dentition	3	2687	0.98 (0.44-1.52)	0
		Mixed dentition	1	1063	0.20 (-0.05-0.45)	NA
		Permanent dentition	5	2381	0.93 (0.29-1.58)	83
	Erosion	Overall OR	7	9012	1.43 (1.01-2.03)	87.9
		Primary dentition	1	837	0.81 (0.45-1.45)	NA
		Permanent dentition	6	8175	1.57 (1.09-2.26)	87.9
Moderate vs High	Caries	Overall OR	11	9710	1.53 (1.17-1.99)	86.2
		Primary dentition	2	1657	3.07 (0.51-18.50)	97.4
		Mixed dentition	2	2855	1.31 (0.95-1.80)	46.5
		Permanent dentition	7	5198	1.34 (1.03-1.75)	73.5
		Overall WMD	4	1820	1.16 (-0.59-2.91)	95.7
		Primary dentition	2	701	0.57 (-0.18-1.67)	0
		Permanent dentition	2	1119	1.57 (-1.08-4.22)	98.6
	Erosion	Overall OR	7	7111	3.09 (1.37-6.97)	97.4
		Primary dentition	2	1164	1.93 (1.49-2.49)	0
		Permanent dentition	5	5947	3.80 (1.19-12.13)	98.2
Never/Low vs High	Caries	Overall OR	8	5743	1.95 (1.57-2.41)	58.8
		Mixed dentition	1	1944	2.36 (1.89-2.95)	NA
		Permanent dentition	7	3799	1.86 (1.46-2.38)	56.5
		Overall WMD	4	1778	1.91 (-0.94-4.75)	97.6
		Primary dentition	2	751	1.09 (-0.40-2.58)	0
		Permanent dentition	2	1027	2.59 (-1.58-6.77)	99.2
	Erosion	Overall OR	10	9564	2.9 (1.32-6.4)	97.5
		Primary dentition	1	916	1.77 (1.20-2.61)	NA
		Mixed dentition	1	154	1.18 (0.47-2.93)	NA
		Permanent dentition	8	8494	3.48 (1.35-9.0)	98
Never/Low vs Moderate/High	**Caries**	Overall OR	17	17892	1.72 (1.41-2.09)	75.9
		Primary dentition	5	5570	2.51 (1.77-3.55)	35.6
		Mixed dentition	2	4152	1.29 (0.53-3.16)	96.7
		Permanent dentition	10	8170	1.59 (1.34-1.89)	47.8
		Overall WMD	11	7360	1.22 (0.48-1.96)	94.7
		Primary dentition	4	2901	1.16 (0.62-1.70)	0
		Mixed dentition	2	1319	0.76 (-0.46-1.98)	87.6
		Permanent dentition	5	3140	1.38 (0.03-2.73)	97.3
	Erosion	Overall OR	13	15927	1.77 (1.28-2.43)	90.9
		Primary dentition	1	965	1.42 (1.02-1.97)	NA
		Mixed dentition	2	1124	2.03 (0.7-5.89)	64
		Permanent dentition	10	13838	1.78 (1.22-2.58)	92.9

CI = Confidence interval; N = Number of participants; I^2 = Test of heterogeneity; OR = Odds-ratio; WMD = Weighted mean difference

Table 2. GRADE assessment for evidence certainty

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with low-level SSB intake	Risk difference with Moderate level SSB consumption
Moderate-level SSB consumption compared to Never/Low-level SSB consumption in the general population					
Dental caries assessed with presence/absence	13920 (16 studies)	⊕⊕⊕⊕ HIGH [a]	OR 1.57 (1.28 to 1.92)	534 per 1,000	109 more per 1,000 (61 more to 154 more)
Dental caries assessed with mean DMFT/dmft	6131 (9 studies)	⊕⊕⊕○ MODERATE	WMD 0.82 (0.38 to 1.26)	-	WMD 0.82 DMFT/dmft higher (0.38 higher to 1.26 higher)
Erosion assessed with presence/absence	9111 (7 studies)	⊕⊕⊕○ MODERATE	OR 1.43 (1.01 to 2.03)	399 per 1,000	88 more per 1,000 (2 more to 175 more)
High-level SSB consumption compared to Moderate-level SSB consumption in the general population					
Dental Caries assessed with presence/absence	9738 (11 studies)	⊕⊕⊕⊕ HIGH [a]	OR 1.53 (1.17 to 1.99)	532 per 1,000	103 more per 1,000 (39 more to 161 more)
Dental Caries assessed with mean DMFT/dmft	1820 (4 studies)	⊕⊕⊕○ MODERATE	WMD 1.16 (0.59 to 2.91)	-	WMD 1.16 DMFT/dmft higher (0.59 lower to 2.91 higher)
Erosion assessed with presence/absence	7111 (7 studies)	⊕⊕⊕⊕ HIGH [b]	OR 3.09 (1.37 to 6.97)	409 per 1,000	272 more per 1,000 (78 more to 419 more)
High-level SSB consumption compared to Never/Low-level SSB consumption in the general population					
Dental caries assessed with presence/absence	5771 (8 studies)	⊕⊕⊕⊕ HIGH [a]	OR 1.95 (1.57 to 2.41)	437 per 1,000	165 more per 1,000 (112 more to 215 more)
Dental caries assessed with mean DMFT/dmft	1778 (4 studies)	⊕⊕⊕○ MODERATE	WMD 1.91 (0.94 to 4.75)	-	WMD 1.91 DMFT/dmft higher (0.94 lower to 4.75 higher)
Erosion assessed with presence/absence	9710 (10 studies)	⊕⊕⊕⊕ HIGH [b]	OR 2.90 (1.32 to 6.40)	265 per 1,000	246 more per 1,000 (58 more to 433 more)
Moderate/High-level SSB consumption compared to Never/Low-level SSB consumption in the general population					
Dental caries assessed with presence/absence	17893 (17 studies)	⊕⊕⊕⊕ HIGH [a]	OR 1.72 (1.41 to 2.09)	367 per 1,000	132 more per 1,000 (83 more to 181 more)
Dental caries assessed with mean DMFT/dmft	7360 (11 studies)	⊕⊕⊕○ MODERATE	WMD 1.22 (0.48 to 1.96)	-	WMD 1.22 DMFT/dmft higher (0.48 higher to 1.96 higher)
Erosion assessed with presence/absence	15927 (13 studies)	⊕⊕⊕○ MODERATE	OR 1.77 (1.28 to 2.43)	264 per 1,000	124 more per 1,000 (51 more to 202 more)

CI: Confidence interval; OR: Odds-ratio; MD: Mean difference. The risk in the exposed group (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the exposure (and its 95% CI).
a. Outcome upgraded by one increment due to presence of dose-response gradient.
b. Outcome upgraded by one increment due to the presence of a large effect.

IN-TEXT FIGURE LEGENDS (both provided in a separate file)

Figure 1. PRISMA flow chart for systematic reviews[19]

Figure 2. Linear and non-linear dose-response curve between amount of daily SSB consumption and the risk of having dental caries